PATENT

Part of 17/2

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

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| In re Application of: | § | |
| J. M. Steinke | § | |
| A.P. Shepherd | § | Examiner: K. Hantis |
| | § | |
| Serial No.: 07/953,680 | § | |
| | § | Group Art Unit: 2505 |
| Filed: September 29, 1992 | § | |
| | § | |
| For: METHOD AND APPARATUS FOR DIRECT SPECTROPHOTOMETRIC MEASUREMENTS IN UNALTERED WHOLE BLOOD | § | Atty. Dkt.: UTSK:142/BAH |

#17½

**CERTIFICATE OF MAILING**
**37 C.F.R. § 1.8**

**I hereby certify that this correspondence is being deposited with the U.S. Postal Service as First Class Mail in an envelope addressed to: Assistant Commissioner of Patents, Washington, D.C. 20231, on the date below:**

October 10, 1995 — David D. Bahler

**Date** **David D. Bahler**

**DECLARATION OF CHARLES F. MOUNTAIN UNDER 37 C.F.R. § 1.132**

Commissioner of Patents
and Trademarks
Washington, D.C. 20231

Sir:

I, CHARLES F. MOUNTAIN, do hereby declare and state:

1. In 1978, Northeastern University conferred on me a Bachelor of Science degree in Mechanical Engineering. I have 23 years of experience in the field of medical product development. I hold several U.S. patents for medical instruments, and am familiar with all of the commercially available blood gas analyzers and co-oximeters now on the market in the United States, or that have been on the market in the United States within the last 23 years.

I currently hold the position of Director of Business Development with Instrumentation Laboratory, a major company that manufactures and sells blood gass analyzers and co-oximeters all over the world. A copy of my resume is attached.

2. I have read the following documents:

A. The above-identified patent application including pending claims 1-36;

B. The Office Action mailed by the United States Patent Office on April 26, 1995;

C. Anderson and Sekelj, "Light-Absorbing and Scattering Properties of Nonhemolyzed blood," *Phys. Med. Bio.*, Vol. 12, 2:173-184, 1967;

D. Brown et. al., U. S. Patent No. 4,134,678;

E. Curtis, U. S. Patent No. 5,064,282.

3. I am a coinventor of the invention disclosed and claimed in U. S. Patent No. 4,134,678 (hereafter "my '678 patent"), mentioned in item D in the previous paragraph. My '678 patent was filed on March 16, 1977, and issued on January 16,1979.

4. In the 5-year period proceeding the filing of my '678 patent, my employer, Instrumentation Laboratory, had a team of highly qualified technical experts attempt to design a spectrophotometric device capable of measuring multiple hemoglobin species. We simultaneously undertook two different

measurement approaches: measurements on unaltered whole blood and measurements on hemolyzed blood. The reason for attempting to develop an instrument to make measurements on unaltered whole blood was that this approach offered significant commercial advantages over a system requiring hemolysis These advantages included 1) lower manufacturing costs, 2) simplification of mechanical and fluidic components by eliminating the processes of hemolysis and dilution, 3) simplification of the calibration of total hemoglobin measurement by eliminating sample dilution, 4) faster analysis, and 5) greater ease of integration with a system for blood gas analysis.

5. I was a member of that design team, and I was aware of the existing state of the technology that dealt with the optical properties of whole blood, and was specifically aware of the Anderson and Sekelj reference, mentioned as item C in the above paragraph 2.

6. At the time the application for my '678 patent was filed, it had already been known for several decades that 1) hemolyzed blood obeyed Beer's Law and thus that hemoglobin species could be measured spectrophotometrically in hemolyzed blood; and 2) light scattering by red blood cells and other components of whole blood prevented making such measurements directly in unaltered whole blood.

7. Despite years of effort that included numerous experiments with unaltered whole blood and various optical designs and strategies, our design team failed in its attempt to devise a means for measuring multiple hemoglobin species directly in unaltered whole blood.

8. Our design team never achieved results in unaltered whole blood that agreed closely with results in hemolyzed blood. In contrast, Table IV on page 40 of the present application makes just such a comparison. To me it is an astonishing accomplishment that the present invention can make measurements in unaltered whole blood that agree, as closely as they do, with those in hemolyzed blood.

9. Instead of continuing our efforts at instrumentation Laboratory to devise a means of measuring multiple hemoglobin species directly in unaltered whole blood, we abandoned this approach for several reasons. First, nothing in our experiments or in the prior art of which we were aware indicated that such an approach was feasible. Second, in the literature of clinical chemistry, it was a well-established understanding at that time that hemolyzing the blood sample was an absolutely necessary prerequisite to measuring multiple hemoglobin species in blood.

10. After abandoning our efforts to devise a means of measuring multiple hemoglobin species directly in unaltered whole blood, we

concentrated our efforts on making the measurements on a hemolyzed blood sample which led to the design of the co-oximeter described in my '678 patent. That device automated the hemolysis of the blood sample and automated the subsequent spectrophotometric analysis. However, that co-oximeter relied completely on prior hemolysis of the blood samples to eliminate light scattering and would not yield valid results without such prior hemolysis.

11. My '678 patent expressly requires hemolysis prior to the spectrophotometric measurement of multiple hemoglobin species. See, for example, my '678 patent, col. 6, lines 41-43; col. 8, lines 2-7 and 21-22; col. 10, lines 8-9; col. 13, lines 55-68; col. 14, lines 16-17; col. 15, line 43; col. 16, lines 8 and 40; col. 17, line 6 and 37, and col. 18, lines 9 and 36-37.

12. I understand that the Office Action dated April 26, 1995 states that my '678 patent discloses "measurements at different wavelengths to calculate several different constituents of blood" and uses this alleged disclosure to reject claims of the above-identified patent application. In my opinion, the use of my '678 patent in this regard is erroneous.

13. Unlike the invention of the above-identified patent application, my '678 patent does not apply to unaltered whole blood. The invention of my '678 patent must hemolyze the blood

sample to eliminate the extreme light scattering that red blood cell (RBCs) cause in undiluted, whole blood, whereas the method of the above-identified patent application, to the best of my knowledge, is the first and only method that has successfully made accurate spectrophotometric measurements of multiple hemoglobin species directly in unaltered, whole blood.

14. In the Office Action dated April 26, 1995, the Examiner mistakenly contends that my '678 patent can be combined with Anderson and Sekelj to render the present invention obvious. I strongly disagree. The Examiner does not understand that Anderson and Sekelj have not deduced the total hemoglobin concentration from optical measurements; they simply have mixed oxygenated red blood cells and saline in various proportions and measured the total hemoglobin concentration by some unstated independent means. Then, by measuring optical density before and after hemolyzing the suspensions of known hemoglobin concentration, they obtain a measure of light scattering in that particular red blood cell suspension. This approach is clearly not practical to determine concentrations of hemoglobin species in unaltered whole blood for several reasons. First, having to measure the optical density both before and after hemolysis is too cumbersome to even consider. Second, any quantity of light scattering determined for one sample most probably would not apply to another sample due to the many factors that make light scattering vary markedly from one clinical blood sample to the

next. Some examples of these many factors are mentioned in the second and third full paragraphs on page 7 of the present application. In my view, anyone reading Anderson and Sekelj would actually be discouraged from even attempting to measure multiple hemoglobin species directly in unaltered whole blood because 1) they show in their Figure 6 that light scattering makes a quantitatively significant contribution in comparison with the Beer's Law absorbance upon which any method would depend, and 2) their conceptual framework (Twersky's idealized formalism) cannot possibly account for the optical behavior of real clinical blood samples. In my view, no combination of my '678 patent with Anderson and Sekelj could possibly yield the present invention, and a close reading of Anderson and Sekelj would discourage anyone from considering such a combination feasibly possible.

15. In the 28 years since the Anderson and Sekelj paper was published, and in the 16 years since my '678 patent was issued, four companies have developed so-called co-oximeters that measure the total hemoglobin concentration and the relative concentrations of four hemoglobin species. These companies are: Instrumentation Laboratory, Ciba Corning, Radiometer and AVL. In each case, the instruments are designed to hemolyze the sample before subjecting the sample to spectrophotometric analysis. The present invention, to my knowledge, is the first and only one to

succeed in making these measurements directly in whole, undiluted blood.

16. As a research and development executive with 23 years of experience with Instrumentation Laboratory, in my view the present invention should not be considered obvious in view of the prior art. Furthermore, in comparison with the existing instruments made by the four companies mentioned in the previous paragraph and as typified by the instrument disclosed in my '678 patent, the present invention has tremendous advantages including: 1) dramatically lower manufacturing costs due to the elimination of chemical or ultrasonic hemolyzers, pumps, and plumbing prone to clogging; (2) non-destructive measurements that allow the sample with intact red blood cells to be subjected to further hematological or other analysis such as measurement of electrolytes or hematological variables; (3) a rugged compact design, and (4) more rapid analysis of samples.

17. I have reviewed performance data on instruments embodying the present invention, including that presented in Table IV on page 40 of the present application, and understand that the present invention is capable of measuring total hemoglobin to an accuracy of less than 0.5 g/dL and the relative concentrations of the individual hemoglobin species to accuracies of 1-2.5%. As an experienced executive in the development of co-oximeters, I can

attest that these accuracies are clinically and commercially acceptable.

18. The prior art references of which I am aware, including items C-E mentioned above in paragraph 2, do not teach one of ordinary skill in this technology, and do not teach me personally, how to make or use the invention disclosed and claimed in the above-identified application. No prior art references of which I aware, nor any combinations of such prior art references, teach to one of ordinary skill in this technology, or to me personally, how to make or use the invention as claimed in the above-identified U. S. patent application. Further, even in view of the scope and content of the disclosure of that prior art, the invention as claimed in the present patent application, as a whole, would not have been obvious at the time the invention was made to a person having ordinary skill in this art.

19. I hereby declare that all of the statements made herein of my own knowledge are true, and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful, false statements and the like are punishable by fine and/or imprisonment under Section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the

validity of the above-identified application, or any patent issuing therefrom.

July 6, 1995
Date

Charles F. Mountain

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Charles F. Mountain
19 Newman Street
Cambridge, MA 02140

## Employment/Experience

1972 - Present Instrumentation Laboratory

- 1991 - Present Director of Business Development

  Responsible for development of new business opportunities. Include setting of product line strategies with Marketing Managers and then formulating search plans to obtain required technologies and products. Have begun formulization of business development process which was not in place previously. Coordinate activities with European division. Have documented design goals of six (6) new products and distributed to R&D.

- 1989 - 1990 Director of Product Planning and Development

  Responsible for new product planning and coordination between R&D groups in Lexington and Milano. Generated and/or reviewed all new product concepts and specifications. Generated the 1990 Strategic Plan. Responsible for business development.

- 1988 - 1989 Program Manager

  Responsible for corporate program management of Phoenix analyzers development in matrix organizational format. Coordinated R&D, Marketing, Manufacturing, Service and Quality Assurance efforts to achieve product release. Also responsible for specification agreement with Europe and initial transfer of Phoenix product. Activities included assisting R&D on the specification of new development programs.

- 1985 - 1988 Director of Product Development - R&D

  Responsible for instrument/system development and continuation engineering in Lexington and Spokane. Included release of 382/482 CO-Oximeter, initiation of Phoenix program, Monarch reliability enhancements and the termination of critical care and sample processing programs. Reduced manpower as required. Implemented CAD systems into development groups. Managed up to 75 engineering professionals.

- 1981 - 1984 Project Manager - R&D

  Managed PLE group (continuation engineering) and development groups. Reduced PLE requirements by >50% over two year period. Responsible for development of small products (e.g. STATSEP). Also took on responsibility for Critical Care and other products/project for discontinuation prior to purchase by Allied.

- 1972 - 1980 Engineer/Senior Engineer/Principal Engineer

  Responsible for mechanical engineering of many varied instruments. Major contributor to development of IL 282 CO-Oximeter, including project leadership at release. Involved with the design of most projects development during this period. Promoted to principal engineer/project leader in recognition of efforts on CO-Oximeter.

## Education

Northeastern University
Boston, MA

A.S., B.E.T. and B.S. in Mech. Engineering. Graduated with highest honors Class Marshall Award (first in class), Alumni Award for Professional Promise.

## Patents and Publications

- Patent 4134678 Automatic Blood Analysis Apparatus and Method (IL 282).
- Patent 4299794 Analytical System for Analyzing $CO_2$ Content of a Fluid (IL 508).
- Patent 4361253 Liquid Transfer Device (Ampule Injector).
- "A Unique Method for the Rapid Separation of Plasma for Whole Blood", K.D. Legg, C. M. Collins, C. F. Mountain; The Journal of Clinical Laboratory Automation, Vol. 3, No. 1, January 1983.

## Personal

- Married with three children.
- Active in community:
  - Coach Little League Baseball.
  - Served on interview committee for City Manager.
  - Advisory Board for Cambridge Police Commissioner.